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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER

EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 11/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/009,261

Applicant(s)

BARTHOLEYNS ET AL.

Examiner

G. R. Ewoldt, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 30 August 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 17-28 is/are pending in the application.
- 4a) Of the above claim(s) 25 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-8, 17-24, 26-28 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's amendment and remarks filed 8/30/05 are acknowledged.

2. Claims 9-16 have been canceled.

Claims 17-28 have been added.

Claim 25 is withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claims 1-8, and newly added Claims 17-24 and 26-28, are being acted upon.

3. Claims 20 and 21 are objected to as depending on canceled Claim 9.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-8, and newly added Claims 17-24 and 26-28, stand/are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As set forth previously, it is unclear how a complex can be formed between an entire tissue extract and a particle. A tissue extract would most likely be a liquid composition comprising soluble and non-soluble components. While a particle might be able to form a complex with a particular component of a tissue extract, it is unlikely, and seemingly impossible, that a complex could be formed with an entire extract. Accordingly, the metes and bounds of the claimed invention are unclear.

Applicant's arguments, filed 8/30/05, have been fully considered but they are not persuasive. Applicant argues that "the invention relates to a molecular complex composed by a tissue extract containing at least one known component and unknown components, and a molecular vector comprising a particle bearing at least two molecules (polypeptides and/or sugars) able to recognize at least one known component of the tissue extract and at least one phagocytic receptor of monocytes-derived cells

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... applicant agrees with Examiner's statement that a molecular complex such as claimed in the present application is not formed between "an entire tissue extract" and a particle. Rather, the molecular complex of the invention involves two or more components of said tissue extract".

It remains the Examiner's position that the claims say (recite) what they say, "molecular complex between a tissue extract ... and a molecular vector" (Claim 1), and "a molecular complex comprising a molecular vector and a tissue extract" (Claims 17 and 26). Applicant's arguments do not change the claims.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-8, and newly added Claims 17-24 and 26-28, stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

As set forth previously, there is insufficient written description to show that Applicant was in possession of the claimed "molecular complex".

The "molecular complex" of the of the instant claims comprises (among other things) any known cellular proteins or sugars, any unknown proteins and sugars, and a carrier "of molecular structure", i.e., anything that binds the known component to a ligand of a phagocytic receptor of a monocyte derived cell. Clearly, the genus of "molecular complexes" encompassed by the claims is essentially unlimited. An adequate written description of the claimed invention would comprise at least a disclosure of a representative number of species of the claimed complexes. A review of the specification, however, discloses no actual "molecular complexes" meeting the limitations of the instant claims. A few of the "known components" of the claimed complexes are disclosed at page 4 of the specification. All of said "known components" are tumor (or more properly, tumor associated) antigens. Clearly this minimal disclosure is not representative of all of the "known components" encompassed by the claims. No species of the "unknown components" of the complex are disclosed, although, again at page 4 of the specification it is discloses that the tissue extracts of the claims contain "normal tissue parts such as tissue membranes, tissue factors, tissue proteins, macroscopic fragments of tissue such as lysates or apoptotic bodies, said tissue being originating from any part of human or animal body or cellular extracts thereof," which would likely be the source of the "unknown components" of the complex. Again, this minimal disclosure, is not representative of all of the "unknown components" of the complex of the claims.

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Additionally, none of the ligands of "phagocytic receptors of a monocyte derived cell" encompassed by the claims are disclosed. Thus, of the three components of the "molecular complex" of the claims, a non-representative number of species of one component is disclosed, and no species of the other two of the components are disclosed.

Regarding the examples, where one might expect to find examples of the claimed invention, neither example discloses a "molecular complex" meeting the limitations of the claims. Example 1 discloses a microparticle, to which annexin V polypeptides are linked, added to a solution of apoptotic bodies. There is no indication of any complex being formed, no disclosure of a "known component" being bound by the particle, nor any disclosure of a ligand of a "phagocytic receptor of a monocyte derived cell". Example 2 discloses that microparticles presenting mannosyl residues at their surfaces are added to a suspension of killed murine hepatocytes and "molecular complexes" are formed. These are clearly not the "molecular complexes" of the instant claims because killed murine hepatocytes are not tissue extracts. Thus, the Example discloses no tissue extract, no bound "unknown component", and no ligand of a "phagocytic receptor of a monocyte derived cell".

Applicant's arguments, filed 8/30/05, have been fully considered but they are not persuasive. Applicant argues that "the unknown components" are inter alia disclosed on page 2, lines 11- 13 and encompass identified tissue antigens, polypeptides or oligosaccharides or an hapten expressed or transfected on the cell membrane of tissues or tumors", "unknown components", are described on page 2 as proteins and saccharides present in cellular extracts of tumors or tissues (lysates, apoptotic extracts). It would therefore be clear to those skilled in the art that such "unknown components" represent non-tagged potential parts of a tissue originating from the potential organs of a human or animal body. They may be macroscopic fragments such as cells, fragments of membranes, lysates or apoptotic bodies, or smaller fragments such as proteins, peptides, glucidic structures".

It remains the Examiner's position that the vast and essentially unlimited number of "known" and "unknown" components of the claimed "molecular complex" are not adequately described in the instant specification. Applicant's reiteration of the brief teachings of the disclosure do not comprise any additional description of the claimed invention.

Applicant further argues "The phrase "phagocytic receptor of monocytes-derived cells" is described on page 2 as being such that "when interacting with a ligand, in this case, the molecular complex, it initiates the uptake of said ligand". Phagocytic receptors of monocytes-derived cells as well as their ligands are well known by a person of ordinary skill in the art. In particular these phagocytic receptors may be mannose

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receptors, receptors for oligosaccharides or Fc receptors, as exemplified in claim 2. Consequently, the ligands in question may be mannose or mannosyl residues, oligosaccharides residues or agonists for Fc receptors". Applicant further argues that the Examples exemplify the molecular vector of the claims.

Applicant appears to be arguing that while just one of the components of the "molecular vectors" of the claims, capable of "recognizing" a phagocytic receptor on monocyte derived cells, is described in the specification (mannosyl residues), the skilled artisan would simply know the rest of said vectors. Further, annexin V appears to be the only disclosed component of the molecular vector that recognizes the known component of a tissue extract (Example 1). An adequate written description of the critical components of a claimed invention requires some sort of actual written description comprising either a representative number of said components, or an adequate written description of common functional and structural features; neither are disclosed in this case. Applicant's assertion that said component would be well-known is not convincing.

8. Claims 1-8, and newly added Claims 17-24 and 26-28, stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that any "molecular complexes" of the instant claims can be made.

As set forth previously, regarding the "molecular complexes" of the instant claims, it is noted (as set forth above) that the complexes are inadequately and unclearly described. It is conceivable, however, that the skilled artisan could make an invention that was inadequately described; but it would be scientifically appropriate then to conclude that significant guidance would be required. A review of the specification discloses that no guidance of any type is given regarding the making of the claimed "molecular complexes". Indeed, the specification merely states repeatedly that the invention "relates" to various methods. At best, then the skilled artisan is left with guessing how to make the claimed invention, and then employing methods of trial-and-error. As methods of trial-and-error provides no particular expectation of success that any particular complexes produced would meet the limitations of the claims, said methods are considered to be unpredictable, thus, necessitating undue experimentation.

Applicant's arguments, filed 8/30/05, have been fully considered but they are not persuasive. Applicant reiterates page 3 of the disclosure, points to Example 1, and directs the Examiner's attention to the new claims.

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Applicant is advised that none of these cites disclose how to make the claimed molecular complex. Broad disclosures of components of the claimed product (indeed, it is unclear if there would be any proteins or polysaccharides that would not be encompassed as possible components of the claimed invention) do not comprise a description of how to make a claimed product.

9. The following are new grounds for rejection necessitated by Applicant's amendment.

10. Claims 17-24 and 26-28 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

- A) the saccharides of the tissue extract (Claim 17),
- B) the mannosylated residues recognizing the mannose or oligosaccharide receptors of monocyte derived cells (Claim 19),
- C) the mannose receptors (Claim 24),
- D) the hepatocyte tissue extract and mannosylated residues (Claim 26),
- E) the cell line M17 (Claim 27), and
- F) the known component hepatocyte and the macrophage with liver tissue specificity (Claim 28).

Applicant cites the original claims and pages 2, 10, and 8-9 of the specification in support of the new claims.

No support has been found for the specific combinations of limitations set forth above. Regarding A), saccharides are disclosed only as part of the unknown component of tissue extracts. Regarding B), C), and D), mannose and mannosylated residues, and E), the cell line M17, are disclosed only in the context of the limitations of Example 1 and not in the generic contexts of the claims. Regarding D) and F), hepatocyte tissue and hepatocytes are disclosed only in the context of the limitations of Example 2 and not in the generic contexts of the claims.

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10. No claim is allowed.

11. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

13. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


11/10/05

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